

REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application. Applicants request reconsideration of the subject application based on the following remarks.

Claims 1 thru 19 are currently pending in the application. Claims 1, 5, 7 and 13 have been amended.

Support for the amendments to the claims can be found throughout the application as filed. No new matter has been added by the amendments to the specification or the claims.

Claims 1-17 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U. S. Patent No. 6,413,544.

Applicants are concurrently filing herewith a Terminal Disclaimer which disclaims, only with regard to claims 1-17, the terminal portion of any patent granted on this application which would extend beyond the expiration of U.S. Patent No. 6,413,544. As such, the basis for this rejection is obviated.

Claims 1-4 and 6-7 were rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Sternberg (J. of Liposome Research, 6 (3), pp. 515-533, 1996), as Sternberg discloses the instant liposomes, containing DOTAP and cholesterol.

Applicants respectfully disagree with the Examiner's assertion. First of all, there is no mention in the Sternberg publication of combining DOTAP with cholesterol to form liposomes. There is mention of complexes of DC (a different cationic lipid) with cholesterol, but not DOTAP. Secondly, the resulting liposome structures of the present invention form invaginated vase-like structures which are entirely unlike the "spaghetti and/or meatball" like structures cited on page 522 of the publication.

Claims 1-14 and 17-19 were rejected under 35 U.S.C. 102(b) as being allegedly anticipated by WO93/25673 wherein liposomes made of DOTAP, cholesterol derivative and DNA are disclosed (Example 2), and further, that the liposomes can be targeted (page 29).

Applicants respectfully disagree with the Examiner's assertions. It should be noted that the claims of the present application have been amended such that all claims recite liposomes which have an invaginated vase-like structure, which is principally due to the novel method of preparing the liposomes of the present invention. These invaginated vase-like structure liposomes offer significant advantages, particularly with regard to the efficiency of delivery. WO93/25673 makes no reference to liposomes having an invaginated vase-like structure. Furthermore, the method of preparing liposomes mentioned in Example 2 is quite different from the present invention. In Example 2 of WO93/25673, the lipids and cholesterol are mixed together, evaporated to dryness, resuspended by vortexing and sonicated. The methods of the present invention involve heating a mixture of lipids and cholesterol, sonicating the mixture and then extruding the lipid components sequentially through filters of decreasing pore size which forms the invaginated liposomes.

With regard to liposomes that can be targeted, page 29 of the WO93/25673 refers to the use of specific cationic lipids to confer the ability of certain liposomes to target the lung. The targeting of liposomes of the present invention involves the use of specific ligands for binding to certain tissue specific proteins, where such ligands are positioned on the surface of the liposomes of the present invention. The two methods of targeting are quite different.

Claims 1-14 and 17-19 are rejected under 35 U.S.C. 102(e) as being allegedly anticipated by Debs (US 5,827,703) wherein liposomes containing DOTAP, a cholesterol derivative and DNA are disclosed (Abstract and Example 2).

Applicants respectfully disagree with the Examiner's assertion. The same argument recited above with regard to WO93/25673 is applicable for Debs, as well, since the liposomes of Debs are prepared by the same method used in WO93/25673. The '703 patent makes no reference to liposomes having an invaginated vase-like structure.

Furthermore, the method of preparing liposomes mentioned in Example 2 is quite different from the present invention. In Example 2 of '703, the lipids and cholesterol are mixed together, evaporated to dryness, resuspended by vortexing and sonicated. The methods of the present invention involve heating a mixture of lipids and cholesterol, sonicating the mixture and then extruding the lipid components sequentially through filters of decreasing pore size which forms the invaginated liposomes.

Claims 1-14-14 and 17-19 were rejected under 102(e) as being allegedly anticipated by Felger (US 5,580,859) wherein liposomes containing DOTAP, cholesterol and nucleic acids are disclosed (Example 6)

Applicants respectfully disagree with the Examiner's assertion. Once again, the method of preparing liposomes in the '859 patent is quite different than the method of the present invention, even though they both may involve sonication. Given the significant differences, the method of preparing liposomes in the '859 patent would not result in producing liposomes with invaginated vase-like structures.

Claims 1-14 and 17-19 were rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Sternberg or Felger cited above.

Applicants respectfully disagree with the Examiner's assertions. Neither Sternberg or Felger mention liposomes with invaginated vase-like structures or the methods by which invaginated vase-like liposomes could be produced. Consequently, one of ordinary skill in the art would not have been motivated to combine the teachings of Sternberg and Felger to achieve invaginated vase-like liposomes of the present invention.

Claims 15 and 16 were rejected under 35 U.S.C. 103 (a) as being unpatentable over Sternberg or Felger or Debs or WO93/25673 cited above, and in further view of Wasan (J. Pharm Sci, 85 (4), PP. 427-433) and Kitaguchi (US 5,206,027). As with the other citations used as a basis of rejection in the current office action, Wasan and Kitaguchi make no mention of invaginated vase-like liposome structures or the methods of preparing them. Consequently, one of ordinary skill in the art would not have been

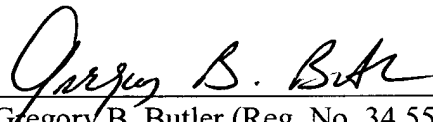
motivated to combine the teachings of Sternberg and Felger and Debs and WO93/25673 and Kitaguchu to achieve invaginated vase-like liposomes of the present invention.

In summary, reconsideration of this application and the allowance of Claims 1-19 of this application as hereinabove amended in response to this communication are respectfully requested for the reasons stated above.

Finally, Applicants believe that additional fees are not required in connection with the consideration of this response to the currently outstanding Official Action. However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge and/or credit Deposit Account No. **04-1105**, as necessary, for the correct payment of all fees which may be due in connection with the filing and consideration of this communication.

Respectfully submitted,

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